BRAZILIAN MINISTRY OF HEALTH PUBLIC CONSULTATION #8 OF 2014
PUBLIC-PRIVATE PRODUCTIVE DEVELOPMENT PARTNERSHIPS

Introduction:

The Biotechnology Industry Organization (BIO) welcomes the opportunity to provide comments to Public Consultation #8 published by the Brazilian Ministry of Health on August 14, 2014 which proposes a new regulation defining the guidelines and criteria for the submission, formation, monitoring and evaluation of PDP (Public-Private Productive Development Partnerships) projects.

BIO is a global not-for-profit industry association representing more than 1,100 companies, universities, research institutions, investors and other entities in the field of biotechnology in more than 30 countries throughout the world, including Brazil. The members of BIO, which range from entrepreneurial companies developing a first product to Fortune 500 multinationals, are involved in the research and development of healthcare, agricultural, industrial and environmental biotechnology products. As the world's largest biotechnology organization, BIO has been involved with governments around the globe in helping to determine global best practices for implementation of biotechnology development policies. It is with this broad experience and global membership pool that BIO shares with the Brazilian Ministry of Health its concerns regarding the newly proposed regulations for PDPs. BIO hopes that this is one of several opportunities to actively engage with the Brazilian Ministry of Health to develop positive and clear regulations that help to create an environment for driving technological advances and spurring innovation in the biopharmaceutical field.

In general Brazil has taken several initiatives to participate actively in and contribute to the global biotechnology industry. Major investments from the government, as well as from domestic and foreign-based members of BIO, have helped to grow Brazil's biotechnology industry. For these reasons, among others, BIO is attentive to legal and regulatory developments in Brazil that affect the biotechnology industry, such as potential changes to the rules for engaging in PDPs. BIO therefore appreciates the opportunity to engage with Brazil's Ministry of Health to share the concerns of its members in order to ensure that decisions are made that continue to strengthen the biotechnology sector, particularly in the health area, in Brazil for years to come.

At the outset BIO commends the Brazilian Ministry of Health for its efforts to revisit its policies and establish clearer rules for forming PDPs. BIO also recognizes that the Brazilian government views the PDP program as strategic to supporting the sustainability of the Universal Healthcare System and as strategic to advancing and incentivizing scientific development, research and technical capacity within Brazil. However, BIO also has identified in the proposed regulations a number of potential issues which may undermine Brazil's goals of making the country more competitive globally in the biopharmaceutical space and that may compromise the most important of all issues, that of providing safe and effective drugs to Brazilian patients.

General Considerations:

- **Unclear definitions:** BIO understands that the Brazilian government will need to develop definitions of key terms, including for example the definition of "PDP", "Technological Portability", "Economicity" and "Basic Productive Process", in order to establish clear rules under this proposed regulation.

- **Transparency and Increased Public Involvement:** Publication of material regarding PDPs should be the rule and not the exception. In addition, no material relating to a normative or rule on PDPs should be published on the Ministry of Health website without also being published by the Ministry of Health in the National Register in an effort to be fully transparent and to give full public notice of the contents of any alteration *t*o the rules. This embodies the spirit of allowing the public to engage on matters that the Brazilian government view as strategic.

- **Impact on prices:** The impact of localization policies such as those reflected in the proposed regulation on the price of drugs is uncertain. In some cases, localization policies may have the effect of driving up the prices of medicines as producers are denied the opportunity to take advantage of economies of scale in their manufacturing operations. Productions costs incurred from manufacturing locally to satisfy government tenders may increase prices, which as a result may potentially affect patient access and care.

- **Multiple PDPs:** BIO understands that clearer rules will need to be provided in order to understand how multiple PDPs for the production of the same product may coexist and how market share may ultimately be divided between competing PDP projects. It is understood, for example, that one of the major advantages of PDPs is to have some degree of market exclusivity in the centralized purchase of strategic products in return for transferring technology but if this exclusivity may potentially be challenged by a second PDP then the Ministry of Health may need to create additional conditions to incentivize the formations of PDPs and control how market share is distributed. In addition to this economic perspective, BIO highlights the potential risks for patient safety that may result from the centralized distribution of biological products that do not have adequate labeling to distinguish products arising from multiple PDPs and that further lack pharmacovigilance plans.

- **IP Rights and PDPs:** Another important issue is the relation of patents with PDPs and how PDPs are to coexist with patents as well as pending patent applications. BIO expects that patent rights will be widely respected by participants of PDPs and that this will be encouraged by the Ministry of Health.

- **Centralization of Purchases:** Throughout the regulation reference is made to products that may potentially be centralized. BIO understands that one of the pillars of the PDP program is to produce strategically important products so that they are purchased centrally by the Ministry of Health in order to attend the

demands of the Universal Healthcare System. It is unclear whether this PDP concept is now being expanded to products for non-centralized purchases.

- **Regional Impact:** In determining whether to approve a PDP project, language has been included in the proposed regulation that suggests that in assessing a PDP project the Ministry of Health will assess the project's contribution to not just local but also regional development. BIO kindly asks for additional clarification on this point and particularly how this potential regional impact is squared with Article 3 of the proposed regulation.

- **Lack of public bidding and potential impact of margin of preference:** Although PDPs are exempt from a bidding process, the citation of Law 12349/2010 in the Whereas clause section suggests that a margin of preference may be applied to PDPs which creates uncertainty as to the PDP formation process, pricing, and the potential impact on public expenses and to a degree the potential undermining of Brazil's stated goals for patient access. BIO understands that all of these factors may contribute to the study of the "economicity" of a PDP project, which may relate to the economic viability or cost-effectiveness of a PDP project.

Specific Concerns by Chapter:
CHAPTER I - GENERAL PROVISIONS:

Article 2 - Definitions

BIO commends the Ministry of Health for defining some key terms for PDPs in this section. However, there are a number of new terms introduced in this regulation that have not yet been used or defined in Brazil. For example, "economicity" is a term used throughout the regulation but which presents uncertainty. The term has no Portuguese definition and suggests cost-effectiveness or economic viability but nonetheless adds elements of uncertainty to the regulation.

BIO also especially recommends that the term "PDP" be defined in this section. As the regulation seeks to provide guidelines and rules for PDPs it would be beneficial to have a clear definition of what a PDP specifically refers to. There is further uncertainty as to the difference between a PDP and PDP for a R&D Project, as mentioned in Article 68, which appears to have different objectives from a traditional PDP to produce a strategically important product.

Currently PDP is defined in Ordinance 837/2012 as a partnership between public institutions and private entities with a view to the access of prioritized technologies, to the reduction of the long-term vulnerability of the Brazilian Universal Healthcare System, and to the centralization and reduction of prices of strategic health products, with the compromise that new strategic and high-aggregate value technologies will be internalized and developed within Brazil.

In addition, there are a number of definitions that do not provide much clarity to the newly introduced terms. For example, PPB – Basic Productive Process and Technological Portability are not well defined in the current draft and BIO would recommend that these definitions be revisited. The definition of PPB for example is highly subjective and varies on a case-by-case basis. Technological Portability on the other hand does not provide what the actual degree of technological transfer is needed to occur with a given institution involved in a PDP and again is subject to a wide-range of interpretations.

Finally, BIO also encourages the Ministry of Health to remove from the proposed regulation the terms radical and incremental innovations. From BIO's perspective, these terms are not helpful in determining whether a PDP should be approved or not. Furthermore, the value of a product in terms of innovation is typically not evident until it has been on the market and compared to existing products.

CHAPTER II - THE LIST OF STRATEGIC PRODUCTS FOR SUS:

Article 4 – List of Strategic Products

BIO recommends that the List of Strategic Drugs that may be subject to a PDP should be open for Public Consultation. This is in line with BIO's general considerations in favor of greater transparency in the formation of and monitoring of PDPs. The Ministry of Health would be able to defend and demonstrate any alterations to the list of strategic drugs and this would be open to public debate and consideration.

In addition, it is recommended that the List of Strategic Drugs be published in a separate, stand-alone Ordinance. Currently, the List of Strategic Drugs is provided for in Ordinance 3089/2013. Since Article 71 of the proposed regulation revokes this Ordinance, BIO suggests that a new list be published in a stand-alone Ordinance to replace the current Ordinance that is to be revoked.

Article 9

BIO reiterates its concern that the list of strategic drugs and other important documents referenced and cited within the proposed regulation are not only made available on the Ministry of Health's webpage but that the list of strategic drugs and other important documents to the proposed PDP regulation, and their updates, are also published in the National Register in an effort to give notice to the public and afford the appropriate legal weight to the documents being cited.

CHAPTER IV- ADMINISTRATIVE PROCESS:

Section I - PDP Project Proposal:

Article 14, § 3

In an effort to have fully transparent rules that allow for full public participation, BIO recommends that the annual calendar of GECIS meetings be published with sufficient notice and that all meetings are open to the public. As the regulation is currently written, it is not made expressly clear that all interested members of the public may be invited to the GECIS meetings.

Article 14, § 4

In addition, BIO supports the Ministry of Health's interest in disclosing results of PDP project proposals that seek to produce the same product. BIO suggests the Ministry of Health elaborate how results will be disclosed and how information may be obtained. BIO would see as reasonable a publication in the National Register of these results with their justifications and reasoning.

Subsection I - Guidelines and Requirements for Drafting of the PDP Project Proposal:

Article 15, I, "b"

BIO suggests that a PDP proposal can only be made by private entities which possess technology to produce the product and that a demonstration of the existence and possession of the technology should be made. Factors that may help in determining whether a company possesses the technology would be perhaps patents or pending patent applications, sanitary market approvals in Brazil, or Phase III clinical trials.

It is understood that if a private entity is at a very early stage of development but still wishes to enter into a PDP, the proper vehicle for participating in PDPs would be through the so-called PDP for Research and Development, such as that described in Article 68 of the proposed regulation.

Article 15, III, "a" and "b"

Again, BIO applauds the Ministry of Health for recognizing the importance of identifying IP rights when evaluating PDP proposals. This provides legal certainty and a positive environment and demonstrates Brazil's commitments to supporting IP rights which are essential in order to drive heavy research and development investments in the health sector to produce innovations to treat conditions in Brazil and around the world.

In this light, BIO recommends that Paragraph III "b" refer to pending patent applications as well as patents. Patent applications represent an expectation of a legal right and should be referenced when submitting PDP proposals given that over the course of the PDP development and phase internalizing the technology the patent application may ultimately be granted generating rights in Brazil that may not have otherwise been considered prior to making the investments in a given PDP project.

BIO also proposes a mechanism by which third parties may be involved in the PDP formation process to claim patent rights.

Finally, given that the PDPs are focused on Brazil-specific development and health issues, BIO requests clarification on the reasoning to inform the countries to which patent protection has been extended for patents or patent applications cited in the PDP project proposal. It follows that According to Article 3, PDPs have exclusively local objectives and hence it is questionable as to why global patent portfolio should be disclosed in order to present a PDP proposal.

Subsection II - Instances of PDP Project Proposal Assessment:

Article 17, VI

BIO expresses concern on the possibility of the existence of more than one PDP for a single product as expressed in Paragraph VI of Article 17.

First and foremost, there are very serious potential safety issues regarding the existence of multiple PDPs for biologics. There are questions, for example, as to how the market share would be divided for biological products and how biological products of different PDPs would be distributed to patients from a centralized purchaser.

On one hand, patients must know which biological drug they are obtaining in order to guarantee safe and effective treatment. According to the WHO Guidelines on Evaluation of Similar Biotherapeutic Products elaborated during the 60th Meeting of thee WHO Expert Committee on Biological Standardization, 19-23 October 2009 (http://apps.who.int/medicinedocs/documents/s19941pt/s19941pt.pdf), a follow-on biologic should be clearly identifiable by a unique brand name. It is understood that biologic products obtained from PDPs by the Ministry of Health may potentially have indistinguishable labeling and therefore it is encouraged that regulations be made that afford for a safe distribution of biologic products with adequate labeling.

Furthermore, this question of distribution of biologic products obtained by PDPs raises additional concerns as to how to establish an adequate post-registration pharmacovigilance reporting mechanism. In accordance with the aforementioned WHO Guidelines on Evaluation of Similar Biotherapeutic Products, it is crucial for patient safety to adequately monitor the use of biologic products through a clear pharmacovigilance plan. However, as there are questions as to how biologic products are to be distributed it is challenging to envision for the industry how a clear pharmacovigilance plan may be instituted in Brazil, which ultimately compromises the health of Brazilians patients.

BIO respectfully raises these concerns to the Ministry of Health to obtain clarification on how patient safety will be addressed with the distribution of centrally purchased biologics of multiple PDPs. BIO also encourages that all biologics to be purchased by the Ministry of Health from PDP projects are to be approved and in compliance with the most recent ANVISA biologic drug regulations.

In addition to the nomenclature, labeling and pharmacovigilance concerns with respect to patient safety, BIO also would like to address the question of interchangeability and encourage the Ministry of Health to review this with ANVISA as there are additional questions concerning how biologic products may be interchangeable with reference biologic products or other non-novel biologics. Strong coordination with ANVISA and with the global community on this issue is encouraged.

Finally, besides the patient safety concerns, BIO recognizes other uncertainties with respect to how the Ministry of Health will manage multiple PDP projects for a single strategic product and how ultimately market share will be divided. BIO kindly requests clarifications on how market exclusivity in the centralized purchase of strategic products may potentially be challenged by the approval of additional PDPs for the same product.

Subsection III - Criteria for Analysis of the PDP Project Proposal:

Articles 23 and 24

Paragraph XIII of Article 23 and Paragraph XI of Article 24 states that one of the factors for determining whether a PDP is to be approved is to measure the impact of this project on local and regional development. BIO is concerned as to the need to measure potential regional impacts in order to determine the merit of a PDP proposal and is curious as to the purpose of this information for the Ministry of Health.

A regional focus for potentially exporting products seems to go against the objectives of the PDP program as defined in Article 3 of the proposed regulation with respect to reducing the vulnerability of the Universal Healthcare System, improving access to health for Brazilians and with respect to reducing the Ministry of Health's deficit. BIO therefore requests clarification on the regional goals of the PDP program.

BIO recognizes as a concern this factor when specifically deciding to choose one PDP over another given that greater weight should be placed, for example, on the quality of the technology being transferred and timeframes for internalizing the technology.

There is also some concern as to whether the Ministry of Health supports the export of products produced by public laboratories through PDPs to other countries. BIO is curious as to the position of the Ministry of Health on this point as well. BIO supports that products are only exported with the express agreement of the company transferring technology and so long as no patents are being violated abroad.

Finally, regarding this concern of how to determine whether to select one PDP over another, Paragraph V of Article 24 cites term "economicity" which as has previously been discussed is an unclear term that is not part of the Portuguese language. BIO is therefore also curious as to how the Ministry of Health will determine whether a PDP provides "economicity".

Subsection IV - Document Support of the PDP Project Proposal Administrative Process:

Article 26, sole paragraph

In an effort to provide for a PDP framework that is transparent and open for the public to review and participate, BIO encourages the Ministry of Health to publish in the National Register the decision in Article 26 as to whether to classify information in the PDP project proposal as confidential by the Secretary of Science, Technology and Strategic Inputs so that interested parties may appeal against the classification in case of disagreement.

BIO encourages the publication of all reports and decisions of the like to encourage public involvement and transparency of the entire PDP process from proposal to full technology integration.

Subsection V - Evaluation and Decision Process of the PDP Project Proposal:

In general, BIO is pleased with the Ministry of Health's efforts in addressing how the Ministry will review and decide to approve or deny PDP project proposals.

Nonetheless, there are a few minor issues which BIO would like to briefly address:

Articles 32, 37 and 38

BIO understands that all of the entities part of a PDP should be encouraged and allowed to participate in any meeting with SCTIE to present oral arguments in defense of its PDP. The current language only allows the public laboratory to participate in this meeting.

Besides informing the public institution of the decision not to approve a PDP, the decision should be informed to all entities involved in a PDP. In addition, the public should be informed of a decision not to grant a PDP with the justification made public as well.
In the event that a PDP is denied, BIO understands that the private entity should have the right to file an administrative appeal against the decision which rejects the PDP project proposal.

Section II – of the PDP Project

Article 48, sole paragraph

In an effort to provide for a PDP framework based on transparency and open public involvement, BIO encourages the Ministry of Health to publish in the National Register the quarterly progress reports sent by the public institutions involved in PDPs to the

Ministry of Health. This will allow interested parties and members of the public to actively follow developments.

CHAPTER V- MONITORING AND EVALUATION

BIO applauds the Ministry of Health for providing comprehensive monitoring rules for PDPs. This section addresses a gap in current PDP regulation. BIO recommends that this section allow again for the publication of reports to site visits over the course of the PDP project.

CHAPTER VII- FINAL DISPOSITIONS

Article 68

As aforementioned, BIO's members are concerned with multiple PDPs for a single product and how the Ministry of Health will address this issue regarding dividing up market share and allocating government resources, besides the question of how to adequately distribute biosimilar biological drugs to patients in a centralized manner without risking patient safety.

This specific article refers to a PDP for an R&D project and BIO would like for the Ministry of Health to issue a separate regulation that will establish the goals and objectives of this specific subset of PDPs.

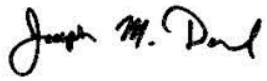
Conclusion

Biotechnological innovation is a complex and challenging process that requires scientific excellence and commitment of significant resources. Through close collaboration with the global biopharmaceutical industry BIO believes that the Ministry of Health will be able to develop new rules for establishing a PDP framework that will strengthen the biotechnology sector, particularly in the health area, in Brazil for years to come.

BIO encourages Brazil to adopt regulations that will help it to become a contributing player in the global biotechnology area. However, policies focused on local and regional markets may undermine Brazil's goals and may have the counter-effect of not helping to make the country competitive. Localization policies may for example impact prices of drugs and potentially elevated costs may impact the ability to adequately meet the demand of the Universal Healthcare System. These policies have potentially questionable effects on economic development and competitiveness in the area and in addressing the most important issue, that of providing Brazilian patients with a supply of safe and effective drugs.

We applaud your efforts to re-evaluate your existing policies and we look forward to working with you to achieve a positive, innovation focused regulatory framework that addresses the short-, medium- and long-term concerns of the Ministry of Health and the Brazilian population.

Respectfully submitted,



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